THE SWISS MODEL OF COMPREHENSIVE ANTIDOTE PROVISION

H. Kupferschmidt*
Swiss Toxicological Information Centre, Associated Institute of the University of Zurich, Zurich, Switzerland

Summary: Antidotes for the treatment of human poisoning are rare but essential medicines. Their provision is a particular challenge because their availability is limited, and many products are not authorized by the government. Their distribution may need special logistic efforts, and their clinical use is difficult because physicians are often not familiar with the indications, ways of administration, specific precautions, and adverse effects. Therefore, the provision of antidotes requires specific expertise, which is usually present in poison center specialists.

In Switzerland, the supply of antidotes is standardized. The antidotes are classified in 3 complementary assortments based on the frequency of poisoning, the place of administration, and logistic criteria. There is a small decentralized assortment for high street pharmacies, an assortment for hospitals with emergency departments, and an assortment for regional centers specialized in antidote supply. In addition to these, there are a number of special assortments: the antidotes stocked in the Swiss Military Pharmacy and in specialized decontamination hospitals for mass casualties, the antivenins for exotic snake bites (antivenin.ch), antidotes for radionuclides, and antidotes for prehospital emergency medical services ("Swiss ToxBox"). All assortments are described in the Swiss Antidotes List.

The antidote network is managed by a working group of hospital pharmacists and staff of the STIC on behalf of the cantons. The group updates and publishes the Swiss Antidotes List annually (www.antidota.ch).

Disclosure of Interest: None declared.

THE RISK–BENEFIT RELATIONSHIP AS A MORAL COMPASS

M. Lievre*
Clinical pharmacology, Faculte de Medecine Lyon Est, Lyon, France

Summary: The re-evaluation of the benefit/risk balance of a medical product as negative often triggers a scandal. The public outrage focuses usually on drug companies, portrayed as cynical and greedy, and regulatory agencies, considered as incompetent. The agencies should have known! Curiously, the attention of the public focuses on efficacy only at the beginning of a product life and turns to a safety-first attitude later, when doubts arise. This illustrates a lack of appreciation of the risk/benefit balance concept in our society, although life is an everlasting risk/benefit game. Most people tend to consider the risk/benefit balance of a medication to be established once and for all at the time of registration. In fact, clinical development favors the evaluation of efficacy, represented by well-defined, prospectively sought end points, assessed with sufficient power, with a predefined statistical risk. In contrast, safety assessment is based on the reporting of mostly unknown events, with a very low power and a high risk of multiplicity. Given these uncertainties, changes in the benefit/risk balance after some time of marketing are not surprising. Such changes may occur with increasing treatment duration or simply with accumulation of data. Once a safety problem has been identified, it is necessary to confront the newly discovered risk with the already-established benefit. This is relatively easy if the benefit was assessed on hard, clinically relevant end points. However, when the benefit was assessed on intermediary or surrogate end points, it does not weigh much against toxicity. In the case of pioglitazone, the decrease in HbA1C accepted as a proof of efficacy did not stand the comparison with a modest increase in the risk of bladder cancer for the French Agency, who suspended the drug marketing authorization. The EMA and the FDA said the drug may prove useful for some patient populations, without defining them. This points to a lack of an evidence-based method of assessment of the benefit/risk balance. Finally, the understanding of the benefit/risk balance varies according to the disease. Cancer is a disease for which there is a high tolerance to safety issues. Some cancer treatments are approved that give a very small increase in survival at the expense of a tremendous increase in grade III to IV toxicity. While some patients may put a very high price on living a few weeks more, a favorable benefit/risk balance for many others is doubtful. In conclusion, the benefit/risk assessment may be improved by a more extensive use of clinically relevant, patient-centered efficacy end points, early use of pharmacoepidemiologic studies in the risk-management plans, and modeling to refine the approach for subpopulations. An effort to educate the public about the risk/benefit issues is necessary, with more objective information in the prescribing information and patient leaflet.

Disclosure of Interest: M. Lievre: grant/research support from NOVARTIS, NOVONORDISK; consultant for MEDTRONIC, TERUMO, ABBOTT, BARD, BOSTON SCIENTIFIC, and CORDIS.

POPULATION PHARMACOGENETICS AND ITS IMPACT FOR PHARMACOVIGILANCE

A. LLerena*
CICAB Clinical Research Centre, Extremadura University Hospital and Medical School, Badajoz, Extremadura, Spain

Summary: There is scientific evidence about the existence of interethnic differences in the metabolism and response to some drugs. The guidelines and dosage recommendations are not necessarily the most appropriate/accurate for populations with different ethnic backgrounds. As a result, there appears to be patients who do not respond to standard pharmacologic treatments designed for other populations or who present adverse drug reactions. These pharmacologic therapeutic failures may be related to genetic differences in the drug metabolism or to other factors linked to the drug mechanism of action.

Genetic factors may underlie individual susceptibility to some types of adverse drug reactions (ADRs). The ability to identify individuals who are susceptible to ADRs has the potential to reduce the personal harm and economic costs of drug-related morbidity. Information from these efforts could be usefully exploited for better disease management and for minimizing harms from ADRs. Information about ethnic specificity of ADR-genetic biomarkers may help to improve the pharmacovigilance strategies in a given population.

In sum, pharmacogenetic studies may help pharmacovigilance, adapting therapeutic recommendations to each country, based on the specific ethnic and cultural identities. This has represented the main goal of the RIBEF Pharmacogenetic Iberoamerican Network, which gathers investigators and clinicians from all over Latin America and some European countries. The RIBEF strategy claims the necessity of developing regional or local strategies to improve the pharmacologic treatment's benefit/risk relationship by developing studies specifically in indigenous and Latino Mestizo populations. Population-oriented pharmacogenetics might enhance global drug use policy and pharmacovigilance at country level according to the ethnical background and cultural specificity, and has a strong potential to improve drug use in populations neglected in clinical trials.

Disclosure of Interest: None declared.